Al kylphenols Category

SECTION ONE

Development of Categories and Test Plans

Chemical Right-to-Know Initiative

HPV CHALLENGE PROGRAM

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Background

On April 13, 2001, Schenectady International, Inc. (SII) submitted Robust Summaries and Test Plans for the Alkylphenols Category (consisting of seventeen (17) alkylphenols) in accordance with SII's commitment to the HPV Challenge Program (AR-201). This submission was posted on EPA's Chemical RTK Website on May 18, 2001. The Environmental Protection Agency (EPA) completed its review of our HPV submission and provided a number of comments to SII in a letter dated November 15, 2001, and posted on EPA's Chemical RTK Website on November 29,200 1.

On April 1, 2002, Schenectady International, Inc. (SII) submitted the revised Robust Summaries and Test Plans for the Alkylphenols Category (consisting of seventeen (17) alkylphenols). This submission was posted on EPA's Chemical RTK Website on April 23, 2002.

On April 8, 2004, Schenectady International, Inc. (SII) volunteered to sponsor Phenol, 4-(1-methylpropyl)- (CAS No. 99-71-8) and submit the robust summary and test plan for inclusion in our mono-substituted para alkylphenols category. In the same letter we informed EPA that CAS No. 27193-28-8 (1,1,3,3-tetramethylbutyl-phenol) that does not specify the position of the octyl group is no longer used and is replaced with CAS No. 140-66-9 (*para*-tertiary octylphenol).

On December 16, 2005, Schenectady International Inc. informed the EPA that since SII has discontinued the manufacture of the HPV chemical *p-(alpha,* alpha-Dimethylbenzyl) phenol (CAS No. 599-64-4) and therefore we will not longer sponsor this chemical under the US EPA HPV program.

On January 5, 2006, Schenectady International Inc. informed the EPA that we discontinued the manufacture of CAS RN: 1806-26-4 (*p*-Octylphenol) as of 2002 and therefore we will no longer sponsor this chemical under the US EPA HPV program. CAS numbers 599-64-4 and 1806-26-4 have been left in the Robust Summaries and Tables at the end of this section to reflect their inclusion in our original submission -- no additional information will be provided on these chemicals.

We have revised our Alkylphenols Category to include the newly sponsored HPV chemical para-sec-butylphenol (CAS No. 99-71-8) and updated the test plan and robust summaries accordingly.

We value EPA's input and have reviewed in detail the specific comments and concerns expressed by the Agency regarding the Alkylphenols Category. *Inter alia,* we have made substantive modifications to our original Robust Summaries and Test Plans. In several instances, EPA requested additional detail related to a study or to studies. Where additional detail was available we have provided it. For ease of locating changes in the robust summaries, data tables, and test plans with respect to the previous submissions, all changes have been highlighted in gray. Where we have found additional data on our compounds for relevant endpoints, we have included it. These additions are indicated by the word "ADDITION" next to the endpoint title

Introduction

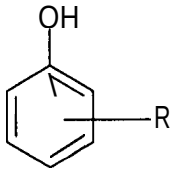
A provision for the use of structure activity relationships (SAR) to reduce testing needs is included under EPA's HPV Program. Specifically, categories may be formed based on structural similarity, through analogy, or through a combination of category and analogy for use with single chemicals. The benefits of using a category approach are numerous and include accelerated release of hazard information to the public, reduction in the number of animals used for testing, and an economic saving as a result of a reduced testing program.

Alkylphenols Category

As defined by EPA under the HPV Program, a chemical category is "a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity." The similarities should be based on a common functional group, common precursors or breakdown products (resulting in structurally similar products) and an incremental and constant change across the category. The goal of developing a chemical category is to use interpolation and/or extrapolation to assess chemicals rather than conducting additional testing with specific consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals.

Relying on several factors specified in EPA's guidance document on "Development of Chemical Categories in the HPV Challenge Program," in which the use of chemical categories is encouraged, the following related chemicals constitute a chemical category with associated subgroupings.

Phenol substituted only with one or more alkyl and/or cumyl group(s).



Where R is one or more alkyl and/or cumyl groups.

List of Alkylphenol Category Members'

Chemical Name	**Abbreviation**	**CAS No.**
2,3,6-Trimethylphenol	TMP	24 16-94-6
p-tert-butylphenol	PTBP	98-54-4
p-sec- butylphenol	PSBP	99-71-8
o-sec-butylphenol	OSBP	89-72-5
2-*tert*-butylphenol	OTBP	88-18-6
p-tert-amylphenol	PTAP	80-46-6
heptyl derivs (*p*-heptylphenol)	PHP	72624-02-3
p-tert-octylphenol	PTOP	140-66-9
p-octylphenol	POP	1806-26-4
2,4-di-*tert*-butylphenol	2,4-DTBP	96-76-4
2,6-di-*tert*-butylphenol	2,6-DTBP	128-39-2
p-(*alpha, alpha*-dimethylbenzyl)phenol[2]	PCP	599-64-4
p-nonylphenol	PNP	84852-l 5-3
2,4-di-*tert*-pentylphenol[3]	2,4-DTAP	120-95-6
p-dodecylphenol	PDDP (TPP)	0555-94-5
4-*sec*-butyl-2,6-di-*tert*-butylphenol	ISONOX 132®	17540-75-9
2,4,6-tri-*tert*-butylphenol	2,4,6-TTBP	732-26-3
2,4-bis(*alpha, alpha*-dimethylbenzyl)phenol[4]	2,4-DCP	2772-45-4

[1] Listed in order of increasing molecular weight.
[2] Commonly referred to as p-cumylphenol.
[3] Commonly referred to as 2,4-di-*tert*-amylphenol.
[4] Commonly referred to as 2,4-di-cumylphenol.

Taking into consideration EPA's comments and category guidance, and subsequent to further evaluation by SII chemists and other experts, the alkylphenols category has been further divided into:

Group I - Ortho-substituted mono-alkylphenols consisting of o-see-butylphenol (OSBP) and 2-*tert*-butylphenol (OTBP)

Group II - Para-substituted mono-alkylphenols consisting of *p-tert*-butylphenol (PTBP), *p-sec*-butylphenol (PSBP), *p-tert*-amylphenol (PTAP), p-heptylphenol (PHP), *p-tert*-octylphenol (PTOP), p-octylphenol (POP), *p-(alpha, alpha*-dimethylbenzyl)phenol (PCP), p-nonylphenol (PNP), andp-dodecylphenol (PDDP or TPP)

Group III - Di- and Tri-substituted mixed alkylphenols consisting of 2,3,6-trimethylphenol (TMP), 2,4-di-*tert*-butylphenol (2,4-DTBP), 2,6-di-*tert*-butylphenol (2,6-DTBP), 2,4-di-*tert*-pentylphenol (2,4-DTAP), 4-*sec*-butyl-2,6-di-*tert*-butylphenol (Isonox), 2,4,6-tri-*tert*-butylphenol (TTBP), and *alpha*-dimethylbenzyl)phenol (2,4-DCP).

Justification for the overall category phenols and Groups I, II, and III

Physical chemistry

All the phenols have a single, common functional group the phenolic hydroxyl. Because alkyl and benzyl groups have a small positive inductive effect all the group phenols are expected to have slightly higher acid dissociation constants (pKa) than phenol (pKa 10.0 at 25°C[5]). Data in a review of the physical chemistry properties of substituted phenols[6] confirms a limited pKa range of 9.9 to 10.9. Thus, none of the alkylphenols will be ionized significantly at environmental or physiological pH's.

Although the overall category phenols do not form a homologous series, values for several of the more important physical chemistry parameters do correlate with molecular weight. In particular water solubility and vapor pressure decrease with increasing molecular weight, and the octanol/water partition coefficient (log Kow) increases. This trend is unmistakable in Group II and Group III substances while the two ortho-substituted materials of the same molecular weight are similar (Tables 1, 2, and 3).

As suggested by EPA, our test plans (Tables 13, 16, and 19) include the experimental determination of water solubility, boiling point, vapor pressure, and octanol/water partition coefficient (Log Kow). In addition, EPIWIN data also has been provided.

[5] The Merck Index, 11th Edition, p. 1150, Merck & Co., Inc., Rahway, N.J.

[6] Mackay, D., Varhannickova, D., Ma, Kuo-Ching & Shiu, Wan-Ying, *Chlorophenols and Alkylphenols: A Review and Correlation of Environmentally Relevant Properties and Fate in an Evaluative Environment,* Chemosphere, Vol 29, No. 6, pp 1155-1224, 1994

Environmental distribution and fate

Direct photolysis is not expected to be a significant route of loss for any of the alkylphenols because of limited absorbance above 290 nm[7]. However, indirect photolysis (atmospheric oxidation) has been estimated for all substances. None of the alkylphenols are expected to be susceptible to abiotic hydrolysis under environmental conditions. Biodegradation study results are available for seven of the seventeen alkylphenols and where lacking, this information has been supplemented by the inclusion of calculated probabilities (made using the prediction program BIOWIN v3.65) for the remainder. In general the laboratory test data showed, as expected, that the lower molecular weight materials with higher water-solubility are more biodegradable than those with higher molecular weights, low solubility and more branching. While not "readily" biodegradable, the alkylphenols as a whole are ultimately inherently, aerobically degradable.

In keeping with EPA's guidance, level III fugacity modeling was conducted for all members of our category and is included in this submission. Changes to the fugacity endpoints will be indicated by "ADDITION" next to the fugacity title. The model reveals that the vast majority of the alkylphenols will be located primarily in the soil and sediment (32-98%) compartment with a few exceptions. The model also suggests that a few lower molecular weight phenols, with correspondingly higher water solubility will also be present in significant quantities in the water compartment (up to 25%). In general the chemicals are not volatile and therefore no significant amounts will be present in the air.

Aquatic toxicity

In response to EPA's observations and suggestions, significant additional aquatic toxicity information has been added to the robust summaries including several chronic fish and invertebrate studies.

The data in Tables 7, 8, and 9 show that the aquatic toxicity of alkylphenols has been extensively investigated. By means of the classification method of Verhaar[8], all the alkylphenols would be classified as Type 2 compounds (polar narcotics). Narcosis, a non-specific mode of toxicity is caused by disruption (perturbation) of the cell membrane. The ability to induce narcosis is dependent on the hydrophobicity of the substance with biochemical activation or reaction involved. Such narcotic effects are also referred to as minimum or base-line toxicity. Polar narcotics such as the category phenols are usually characterized by having hydrogen bond donor activity and are thought to act by a similar mechanism to the inert, narcotic compounds but exhibit above base-line toxicity. In fact, a

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[7] For example p-methylphenol, a typical alkylphenol, has molar absorptivities of 18 l/mol-cm at 297.5 nm and only 1 l/mol-cm at 3 12.5 nm (Smith, J.H. et al, *Environmental Pathways of Selected Chemicals in Freshwater Systems: Part II. Laboratory Studies,* EPA-600/7-78-074, May 1978. Cited in Lyman, W.J., Reehl, W.F. and Rosenblatt, D.H., *Handbook of Chemical Property Calculation Methods,* McGraw-Hill, Inc., Washington, 1990, page 8-38).

[8] Verhaar, H.J.M. van Leeuwen, C.J. and Hermens, J.L.M., *Classifying Environmental Pollutants. I: Structure-Activity Relationships for Prediction of Aquatic Toxicity,* Chemosphere (25), pp 471 – 49 1 (1992).

large number of alkylphenols have been evaluated as intravenous anesthetic agents'. While the structure-activity relationships were found to be complex, the anesthetic potency and kinetics appeared to be a function of both the lipophilic character and the degree of steric hindrance exerted by *ortho* substituents. Less steric hindrance resulted in lower potency, while greater crowding led to complete loss of anesthetic activity and greater lipophilicity resulted in slower kinetics. These data support the notion that the alkylphenols behave as polar narcotics. In addition, the anesthetic activity/potency differences seen with varying structure and placement of substituents strongly supports the division of alkylphenols category into the *ortho, para*, and di/tri-substituted groups (i.e. Group I, II and III, respectively).

In addition to the available experimental values for the different aquatic toxicity endpoints, ECOSAR[10], was also used for calculating aquatic toxicity values (Tables 7, 8 and 9). To be sure, the alkylphenols demonstrate varying degrees of aquatic toxicity. As might be expected for polar narcotic type substances, the aquatic toxicities for the alkylphenols appears to be related to their degree of lipophilicity and increases basically in line with log Kow. Given the apparent lack of structural specificity associated with these endpoints, it is reasonable to assume (where experimentally determined data are not available) that the toxicity of a particular alkylphenol will be comparable to that of another with like lipophilicity. The ECOSAR data in many instances largely supports the available experimental data. With the additional aquatic toxicity data previously noted, further testing is not planned at this time (Tables 14, 17, and 20).

Mammalian toxicity

SII believes it reasonable to consider the mutagenic potential of all the alkylphenols together. The only functional group is the phenolic, which is not a structural alert for mutagenicity. The data support this, since the results of genotoxicity testing are uniformly negative for all twelve substances examined (Tables 10, 11, and 12).

Similarly, we believe the acute (single-dose) toxicity on seventeen of the alkylphenols also shows consistency, with LD_{50} values ranging from approximately 1000 mg/kg to over 2000 mg/kg. These data demonstrate a very low level of acute systemic toxicity and do not suggest any unique structural specificity, despite the general tendency for the chemicals to be, at least, irritants to skin (Tables 10, 11, and 12).

A useful range of repeat-dose toxicity data is available for five of the category members. While EPA commented that several of these were inadequate because of a single dose level (two studies on PTBP), the data nevertheless provide useful insight and are part of the IUCLID database. The available studies for the three groups range from 28-day and 90-day general toxicity studies, through developmental toxicity and reproductive/developmental

[9] James, R., and Glen, J.B. (1980), Synthesis,biological evaluation, and preliminary structure-activity considerations of a series of alkylphenols as intravenous anesthetic agents. *J. Med. Chem.* 23, 1350-1357.
[10] ECOWIN v.0.99e. ECOSAR Classes for Microsoft Windows, United States Environmental Protection Agency.

screening, to recently conducted multigeneration reproductive studies and are summarized in Tables 10, 11, and 12.

The subdivision of the category alkylphenols into and the di/tri-substituted mixed members is supported by several published investigations. In assessing antimicrobial and antifouling activity of twenty-three alkylphenols, a significant difference was noted between *para* and ortho-substituted materials". In particular, biological activity was found to vary parabolically with increasing hydrophobicity of the *para*-substituent while introduction of a bulky substituent at the o&o-position resulted in a very significant decrease in antimicrobial, antifouling, and membrane-perturbation potency. Several alkylphenolic analogs of butylated hydroxytoluene (BHT) were examined for hepatotoxicity in mice depleted of hepatic glutathione[12]. The structural requirement of both hepatic and pulmonary toxicity was a phenol ring having benzylic hydrogen atoms at the para position and an ortho-alkyl group(s) that moderately hinders the phenolic hydroxyl group. It is noteworthy that in this model, neither TTBP nor 2,6-DTBP showed either hepatic or pulmonary toxicity. Lastly, important differences were observed in gene activation (recombinant yeast cell assay – Lac-Z reporter gene) between ortho-substituted and *para*-substituted alkylphenols[13].

For the overall category of alkylphenols, the dosage at which the relatively mild general toxicity appears tends only to fall below 100 mg/kg/day with extended treatment, with an overall NOAEL for the category of approximately 20 mg/kg/day. No unusual and no apparent structurally unique toxicity is evident.

Repeat dose studies on OTBP and PTBP suggest the forestomach to be the main organ affected. OTBP also appears to have a mild (though statistically significant) protective effect against benzo[a]pyrene induced forestomach tumors. Long-term treatment with high dietary dose levels of PTBP caused hyperplastic changes in the forestomach epithelium of rats and hamsters, a likely consequence of the irritancy of the material. The relevance of this for human hazard is doubtful, particularly since there is no analogous structure in humans to the forestomach of rodents.

There was no evidence of an effect on reproductive function at dosages up to 150 mg/kg. One reproductive screening study reported increased 'breeding loss' and also reduced pup weight gain and survival in early lactation at 750 mg/kg/day. It is reasonable to assume that these effects were secondary to "severe toxic symptoms" reported in the dams at this dosage. Other than an indication of a very mildly estrogenic effect of PNP at a high dose levels (200-300 mg/kg/day) no effect on development was seen in a multigeneration study.

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[11] Etoh, H., Ban, N., Fujiyoshi, J., Murayama, N., Sugiyama, K., Watanabe, N., Sakata, K., Ina, K., Miyoshi, H., and Iwamura, H. (1994). Quantitative analysis of the antimicrobial activity and membrane-perturbation potency of antifoulingparu-substituted alkylphenols. *Biosci. Biotech. Biochem.* 58(3), *467-469.*

[2] Mizutani, T., Nomura, H., Nakanishi, K., and Fujita, S. (1987). Hepatotoxicity of butylated hydroxytoluene and its analogs in mice depleted of hepatic glutathione. *Toxicol. Appl. Pharmacol 87,* 166-l 76.

[13] Schmieder, P.K., Aptula, A.O., Routledge, E.J., Sumpter, J.P., and Mekenyan, O.G. (2000) Estrogenicity of alkylphenolic compounds: a 3-D structure-activity evaluation of gene activation. *Environ. Toxicol. Chem.* 19(7), 1727-1740.

Within the *para*-substituted group of nine alkylphenols, repeat dose and reproductive data are available for three substances (PTBP, PTOP, and PNP) and testing of PCP is underway (by another sponsor). two members of this group have SII's category as no longer produced by SII, reducing group size to seven. Thus, data is or will be available on four of the seven members. It is also likely that as many as three members of the di- and tri-substituted mixed alkylphenol group will also no longer be HPV and not likely to become HPV again. Given this and other factors, SII requests a technical discussion with EPA regarding any additional mammalian toxicity testing.

ROBUST SUMMARIES

Physical/Chemical Elements

Notes on calculations etc.
Calculated values for the physical chemistry properties of the category phenols were determined specifically for this HPV submission.

Where an experimental value was available this has been included in a Robust Summary in preference to a calculated value. The single apparent exception to this is for the water solubility of *p*-nonylphenol (CAS No. 84852-15-3) where Summaries containing both the calculated and experimental values have been included because the latter was for solubility in seawater.

All calculated values were obtained using one of the SYRACUSE chemical properties prediction programs run using the interface program EPIWIN v3.

Water solubility values were calculated using log Kow values obtained from the program KOWWIN v1.63.

Environmental Fate and Pathway Elements

Photodegradation
In the absence of experimental data on the direct aqueous photolysis of the category phenols the reported half-life for *p*-cresol (4-methylphenol), a related substance, has been included in all the robust summaries under the heading "Other".

Level III Fugacity Calculations
Water solubility, log Kow, vapour pressure and melting point values were taken from the Physical/Chemical Elements Robust Summaries. That is to say experimental values were used in preference to those calculated.

Ecotoxicity Elements
The aquatic toxicity prediction program ECOSAR v0.99e (g) (run with the interface program EPIWIN v3(3.12)) was used to calculate values for the endpoints: Fish LC50 (96-hr), Daphnid EC50 (48-hr) and Algae EC50 (96-hr). All of these results have been reported in Robust Summaries. Calculated log Kow values obtained from the program KOWWIN were used throughout.

TABLE 1 – Physical Chemistry Properties of Ortho-Substituted Mono-Alkylphenols

Phenol	CAS No.	M w	M.Pt. (°C)		B.Pt. (°C)		V.P. (Pa)		Log Kow		Water Sol. (mg/l)	
			Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.
o-sec-Butylphenol	89-72-5	150	39	14	237	224	2.31	NA	3.46	3.27[1]	319	NA
2-*tert*-Butylphenol	88-18-6	150	37	-7	230	223	3.57	12	3.42	331	344	N A

The following programs were used for calculations:
Melting point, boiling point & vapor pressure: MPBWIN v1 .30
Water solubility WSKOW v1.33
Log Kow: KOWWIN v1 63
The above programs were run using the interface program EPIWIN v3

Numbers have been rounded and the mid-point reported for ranges
Calculated results have been included in the robust summaries only when no experimental result was available. All calculations were performed specifically for this HPV submission
All water solubility calculations were performed using log Kow values obtained using the program KOWWIN v1.63.

[1] Value from KOWWIN database

TABLE 2 – Physical Chemistry Properties of Para-Substituted Mono-Alkylphenols

Phenol	CAS No.	MW	M.Pt. (°C)		B.Pt. (°C)		V.P. (Pa)		Log Kow		Water Sol. (mg/l)	
			Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.
p-tert-Butylphenol	98-54-4	150	37	100	230	237	3.57	0.5	3.42	3 31	344	800
p-sec-Butylphenol	99-71-8	150		56		239	1.12	0.49	3.46	3.08	674.2	960
p-tert-Amylphenol	80-46-6	164	48	95	248	263	1.04	NA	3 91	4.03	113	168
Heptyl derivs (*p*-heptylphenol)	72624-02-3	192	73	NA	296	256-280	0 037	0.0113	5.01	4.5	9.65	12.2
p-tert-Octylphenol	140-66-9	206	73	81	281	282	0.091	0.21	5.28	4 12	4.82	18
p-Octylphenol	1806-26-4	206	83	NA	311	296	0.013	NA	5.50	NA	3.11	N A
p-(*alpha, alpha*-Dimethylbenzyl)phenol	599-64-4	212	103	72	328	335	0.0030	NA	4 12	NA	43.3	N A
p-Nonylphenol	84x52-15-3	220	90	25	316	310	0.0080	0.0046	5 92	3.28 3.8-4.77	1.16	3 93'
p-Dodecylphenol	2 10555-94-S	262	102	-9	330	308	0.0028	9.19×10^{-5}	7 17	7.14	0.058	2.1

The following programs were used for calculations:
Melting point, boiling point & vapor pressure: MPBWIN v1.30
Water solubility: WSKOW v1.33
Log Kow. KOWWIN v1.63
The above programs were run using the interface program EPIWIN v3

Numbers have been rounded and the mid-point reported for ranges
All calculations were performed specifically for this HPV submission
All water solubility calculations were performed using log Kow values obtained using the program KOWWIN v1.63

[1] Seawater

TABLE 3 – Physical Chemistry Properties of Di- and T&Substituted Mixed Alkylphenols

Phenol	CAS No.	M w	M.Pt. (°C)		B.Pt. (°C)		V.P. (Pa)		Log Kow		Water Sol. (mg/l)	
			Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.	Calc.	Exptl.
2,3,6-Trimethylphenol	24 16-94-6	136	41	65	230	222	3.31	<10	3.15	2.72	668	1420
2,4-Di-*tert*-butylphenol	96-764	206	77	57	281	264	0.082	1.0	5.33	NA	4.32	12
2,6-Di-*tert*-butylphenol	128-39-2	206	77	37	281	253	0.082	1.01	4.48	45	23 0	4.11
2,4-Di-*tert*-pentylphenol	120-95-6	234	89	26	311	NA	0.01 |	N A	6.31	NA	0.444	N A
4-*sec*-Butyl-2,6-di-*tert*-butylphenol	17540-75-9	262	102	47	330	275	0.0028	NA	6.43	NA	0.248	NA
2,4,6-Tri-*tert*-butylphenol	732-26-3	262	104	131	325	278	0.0035	0.088	6 39	6.06	0 267	NA
alpha-dimethylbenzyl)phenol	2772-45-4	330	172	65	436	>300	7.8E-07	NA	6.73	NA	0.055	NA

The following programs were used for calculations
Melting point, boiling point & vapor pressure: MPBWIN v1.30
Water solubility: WSKOW v1 33
Log Kow: KOWWIN
The above programs were run using the interface program EPIWIN v3

Numbers have been rounded and the mid-point reported for ranges.
Calculated results have been included in the robust summaries only when no experimental result was available All calculations were performed specifically for this HPV submission.
All water solubility calculations were performed using log Kow values obtained using the program KOWWIN v1.63.

TABLE 4 - Level III Fugacity Modeling Results for Ortho-Substituted Mono-Alkylphenols

Phenol	CAS No.	MW	Air %	Soil %	Water %	Sediment %
o-sec-Butylphenol	89-72-5	150	0.555	74	24.8	0.69
2-*tert*-Butylphenol	88-18-6	150	0.31	81.9	17	0.79

TABLE 5 - Level III Fugacity Modeling Results for Para-Substituted Mono-Allqlphenols

Phenol	CAS No.	MW	Air %	Soil %	Water %	Sediment %
p-tert-Butylphenol	98-54-4	150	0.26	80.5	18.4	0.85
p-sec-Butylphenol	99-71-8	1.50	0.56	73.8	25.1	0.488
p-tert-Amylphenol	80-46-6	164	0.25	79.4	17.1	3.27
p-tert-Octylphenol	140-66-9	206	0.17	53.3	9.07	37.5
p-Octylphenol	1806-264	206	0.32	48	f2.4	39.3
p-(alpha, alpha-Dimethylbenzyl)phenol	599-64-4	212	0.17	80	15.1	4.72
p-Nonylphenol	84852-15-3	220	0.09	36.9	4.47	58.5
p-Dodecylphenol	210555-94-5	262	0.02	97.7	0.008	2.17

TABLE 6 Level III Fugacity Modeling Results for Di- and Tri-Substituted Mixed Alkylphenols

Phenol	CAS No.	M w	Air	Soil	Water	Sediment
			%	%	%	%
2,3,6-Trimethylphenol	24 16-94-6	136	0.10	78.1	21.6	0.24
2,4-Di-*tert*-butylphenol	96-76-4	206	0.15	55.8	9.94	34.1
2,6-Di-*tert*-butylphenol	128-39-2	206	0.17	63.9	12.3	23.6
2,4-Di-*tert*-pentylphenol	120-95-6	234	0.08	32	3.06	64.8
4-*sec*-Butyl-2,6-di-*tert*-butylphenol	17540-75-g	262	0.12	32.7	2.03	65.1
2,4,6-Tri-*tert*-butylphenol	732-26-3	262	0.16	36.3	2.84	60.7
	2772-45-4	330	0.03	35	I.64	63.3

TABLE 7 - Summary of Acute Aquatic Toxicity Data for Ortho-Substituted Mono-Alkylphenols

Phenol	CAS No.	M w	Calc. log Kow	Fish (96h LC50) Calc.	Fish (96h LC50) Exptl.	Daphoid (48h EC50) Calc.	Daphoid (48h EC50) Exptl.	Algae (96h EC50) Calc.	Algae (96h EC50) Exptl.
o-sec-Butylphenol	89-72-5	150	3 4 6	2.8	NA	20	1.3 (shrimp)	3.8	NA
2-*tert*-Butylphenol	88-l 8-6	150	3 4 2	2.9	15.5'	2.1	2.4 (shrimp)	4.1	NA

Toxicities were calculated by the program ECOSAR v0.99e using log Kow values estimated by KOWWIN v3. Both programs were run using the interface program EPIWIN.
All toxicity endpoint values are in mg/l. Some values have been rounded and mid-points reported for ranges.

'Result from a study that used a formulation of 2-*tert*-butylphenol.

TEXT = Addition since original submission

TABLE 8 - Summary of Acute Aquatic Toxicity Data for Para-Substituted Mono-Alkylphenols

Phenol	CAS No.	MW	Calc. log Kow	Fiih (96h LC50) Calc.	Fiih (96h LC50) Exptl.	Daphnid (48h EC50) Calc.	Daphnid (48h EC50) Exotl.	Algae (96h EC50) Calc.	Algae (96h EC50) Exotl.
p-tert-Butylphenol	98-54-4	150	3.42	2.9	5.14	2.1	3.9	4.1	22.3 (72 hr)
							6.7		
p-sec-Butylphenol	99-71-8	150	3.46	2.78	0.74	2.115	1.8 (96 hr) (shrimp)	3.81	
p-tert-Amylphenol	80-46-6	164	3.91	1.6	NA	1.5	1.7 (96 hr) (shrimp)	1.7	N A
Heptyl derivs (p-heptylphenol)	72624-02-3	192	5.01	0.40	0.85	0.61	0.6 (96 hr) (shrimp)	0.21	25
p-tert-Octylphenol	140-66-9	206	5 28	0.29	0.25	0.51	0.27	0 13	1.9
					0.26 (diff. Species)		0.26 (24 hr) 0.013(96hr)		1.1 (72 hr)
p-Octylphenol	1806-26-4	206	5.50	0.21	NA	041	NA	0.082	N A
	599-644	212	4 12	1.5	NA	1.6	NA	14	N A
p-Nonylphenol	84852-l 5-3	220	5 92	0.13	0.3 1	0.30	0.14	0.037	0.41
					0.128		0.085		0.027
							0.043 (96 hr mysid)		0.0563 (72hr)
p-Dodecylphenol	210555-94-5	262	7.17	0.025	0.14	0.11	0.093	0.003	0.77 (72 hr)
							0.15 (96 hr shrimp LC50)		

Toxicities were calculated by the program ECOSAR v0 99e using log Kow values estimated by KOWWIN v1.63. Both programs were run using the Interface program EPIWIN v3
All toxicity endpoint values are in mg/l Some values have been rounded and nud-points reported for ranges. TEXT = Addition submission

TABLE 9 ▪ Summary of Acute Aquatic Toxicity Data for Di- and Tri-Substituted Mixed Alkylphenols

Phenol	CAS No.	M w	Calc. Log Kow	Fiih (96h LC50) Calc.	Fiih (96h LC50) Exptl.	Daphnid (48h EC50) Calc.	Daphnid (48h EC50) Exptl.	Algae (96h EC50) Calc.	Algae (96h EC50) Exptl.
2,3,6-Trimethylphenol	24 16-94-6	136	3.15	3.9	16 8.2	2.5	126'	6.4	19'
2,4-Di-*tert*-butylphenol	96-76-4	206	5.33	0.27	I.8 (48hr)	0.48	NA	0.12	NA
2,6-Di-*tert*-butylphenol	128-39-2	206	4.48	0.90	7.6 10, 1.4	1.1	1.7' .45	0.65	1.2
2,4-Di-*tert*-pentylphenol	120-95-6	234	6.31	0.076	NA	0.22	NA	0018	N A
4-*sec*-Butyl-2,6-di-*tert*-butylphenol	17540-75-9	262	6.43	0.072	NA	0.22	NA	0.016	NA
2,4,6-Tri-*tert*-butylphenol	732-26-3	262	6.39	0.076	NA	0.226	N A	0.017	N A
2,4-	2772-45-4	330	6.73	0.059	NA	0.21	NA	0011	NA

Toxicities were calculated by the program ECOSAR v0.99e using log Kow values estimated by KOWWIN v1.63 Both programs were run using the interface program EPIWIN v3
All toxicity endpoint values are in mg/l. Some values have been rounded and mid-points reported for ranges.
[1]24h
[2]72h

TEXT = Addition since original submission

TABLE 10 - Available Data on Mammalian Toxicity of Ortho-Substituted Mono-Alkylphenols

Phenol	CAS No.	Acute Toxicity (oral, mg/kg)	Irritancy, skin (eye)	Genetic Toxicity	Repeated-dose Toxicity	Reproductive Toxicity	Developmental Toxicity
o-sec-Butylphenol	89-72-5	>200, <2000 2700	Corrosive	Neg	NA	NA	NA
2-*tert*-Butylphenol	88-18-6	789 oral, rat	Corrosive	Neg	NA	NA	NA

Neg = Negative - = No data available

TEXT = Addition since original submission

TABLE 11 - Available Data on Mammalian Toxicity of Para-Substituted Mono-alkylphenols

Phenol	CAS No.	Acute Toxicity (oral, mg/kg)	Irritancy, skin (eye)	Genetic Toxicity	Repented-dose Toxicity	Reproductive Toxicity	Developmental Toxicity
p-tert-Butylphenol	98-544	>2000 4000	Imtant	Neg*	Hamster 20 week, Rat 1 year: EL 15000 ppm OECD 422, Rat: NOAEL = 200 mg/kg	Yeast Screen $1.5x10^6$ <estradiol No effects, 200 mg/kg, fem. 14d prior to mating - d4 lactation	NA
p-sec-Butylphenol	99-71-8	1650	Corrosive	Neg.	N A	Yeast Screen $3.75x10^6$< estradiol	NA
p-tert-Amylphenol	80-46-6	1830	Corrosive	Neg	N A	NA	N A
Heptyl derivs (p-heptylphenol)	72624-02-3	>200, <2000	Imtant (Irritant)	Neg	NA	NA	N A
p-tert-Octylphenol	140-66-9	22000 2200	Mild irritant (Irritant)	Neg	Rat 90d: NOAEL 30 ppm EL 300 ppm	Rat 2gen: NOAEL 200 ppm (systemic tox.), 2000 ppm (repro.tox.) EL 2000 ppm Yeast Screen $7x10^6$ < estradiol	N A
p-Octylphenol	1806-26-4	1200	N A	NA	NA	NA	N A
p-(alpha, alpha-Dimethylbenzyl)phenol	599-64-4	1770	N A	Neg	NA	NA	NA
p-Nonylphenol	54852-15-3	1882	Corrosive (Imtant)	Neg	Rat 28d: NOAEL 100 mg/kg/d EL 400 mg/kg/d Rat 90d: NOAEL 50 mg/kg/d EL 150 mg/kg/d	Rat 3gen: NOAEL (systemic & repro. Tox.) 200 ppm *ca* 20 mg/kg/d EL (repro. Tox) 650 ppm *ca* 50 mg/kg/d 3-6 orders of magnitude < estradiol	Rat: MatNOAEL 75 mg/kg/d DvNOAEL 300 mg/kg/d MatEL 300 mg/kg/d
p-Dodecylphenol	210555-94-5	2100	N A	NA	NA	N A	NA

* Overall considered negative, although a coul questionable results see added details in rob summary // EL = ffect level // MatEL = Maternal effect level // NOAEL = No-adverse effect level // Dv = Developmental // Mat = maternal // Neg = Negative // NA = No data available // TEXT = Addition submission

TABLE 12 ▪ Available Data on Mammalian Toxicity of Di- and T&Substituted Mixed Alkylphenols

Phenol	CAS No.	Acute Toxicity (oral, mg/kg)	Irritancy, skin (eye)	Genetic Toxicity	Repeated-dose Toxicity	Reproductive Toxicity	Developmental Toxicity
2,3,6-Trimethylphenol	24 16-94-6	>2000	NA	Neg	NA	NA	NA
2,4-Di-*tert*-butylphenol	96-76-4	1500	Irritant	NA	NA	NA	NA
2,6-Di-*tert*-butylphenol	128-39-2	>5000	Irritant	Neg	Rat 28d: NOAEL 15 mg/kg/d EL 100 mg/kg/d	Rat421: NOAEL 150 mg/kg/d MatEL 750 mg/kg/d	
2,4-Di-*tert*-pentylphenol	120-95-6	920	NA	NA	NA	N A	
4-*sec*-Butyl-2,6-di-*tert*-butylphenol	17540-75-g	4800	NA	Neg	NA	NA	NA
2,4,6-Tri-*tert*-butylphenol	732-26-3	1670 (males) 1610 (females)	NA	NA	Rat 24 months. NOAEL 30 ppm Dogs 11 days: increased liver metabolism above 50 mg/kg/d + some autonomic signs at 450 mg/kg/d	NA	N A
2,4-	2772-45-4	N A	Irritant	NA	NA	NA	NA

EL = Effect level MatEL = Maternal effect level NOAEL = No-adverse effect level Neg = Negative • = No data available

TEXT = Addition since original submission

TABLE 13 - Ortho-substituted Mono-alkylphenol Test Plan for Physical Chemistry Endpoints

Phenol	CAS No.	Physical Chemistry Properties				
		Melting Point	Boiling Point	Vapour Pressure	Log Kow	Water Solubility
o-sec-Butylphenol	89-72-5	D	D	D	D	D
2-*tert*-Butylphenol	88-18-6	D	D	D	D	D

Key : C = endpoints fulfilled using calculated data D = endpoints fulfilled using adequate existing experimental data T = Testing Proposed

TEXT = Revision

TABLE 14 - Ortho-substituted Mono-alkylphenol Test Plan for Environmental Fate and Ecotoxicity Endpoints

Phenol	CAS No.	Environmental Fate and Pathway				Ecotoxicology		
		Photo-degradation	Stability in water	Transport/ Distribution – fugacity model	Biodegradation	Acute Fish	Acute Algae	Acute Invertebrate
o-sec-Butylphenol	89-72-5	C	*	C	S	C	C	C/D
2-*tert*-Butylphenol	88-18-6	C	*	C	S	C/D	C	C/D

Key: * = although no studies on abiotic hydrolysis were found, no testing is proposed because the category phenols do not possess that are regarded as being susceptible to hydrolysis under

D = endpoints fulfilled using adequate existing experimental data C = endpoints fulfilled using calculated data S = endpoints fulfilled using category approach (read across)

TEXT = Revision

TABLE 15 - Ortho-substituted Mono-alkylphenol Test Plan for Mammalian Toxicity Endpoints

Phenol	CAS No.	TOXICOLOGY					
		Acute toxicity	**Genetic toxicity - bacterial**	**Genetic toxicity – non bacterial – *in vivo***	**Genetic toxicity – non bacterial – *in vitro***	**Repeated toxicity**	**Repro/ Developmental Toxicity**
o-sec-Butylphenol	89-72-5	D	D	S	S	S	S
2-*tert*-Butylphenol	88-18-6	D	D	S	S	S	S

Key: S = endpoints fulfilled using category approach (read across)
D = endpoints fulfilled using adequate existing experimental data

TEXT = Revision

TABLE 16 - Para-substituted Mono-alkylphenol Test Plan for Physical Chemistry Endpoints

Phenol	CAS No.	Physical Chemistry Properties				
		Melting Point	Boiling Point	Vapour Pressure	Log Kow	Water Solubility
p-tert-Butylphenol	98-54-4	D	D	D	D	D
p-sec-Butylphenol	99-71-8	D	D	D	D	D
p-tert-Amylphenol	80-46-6	D	D	D	D	D
Heptyl derivs (p-heptylphenol)	72624-02-3	C	D	D	D	D
p-tert-Octylphenol	140-66-9	D	D	D	D	D
p-Octylphenol	1806-26-4	C	D	D	D	D
p-(alpha, alpha-Dimethylbenzyl)phenol	599-64-4	D	D	D	D	D
p-Nonylphenol	84852-15-3	D	D	D	D	D
p-Dodecylphenol	210555-94-5	C	D	D	D	D

Key C = endpoints fulfilled using calculated data D = endpoints fulfilled using adequate existing experimental data T = Testing Proposed

TEXT = Revision

TABLE 17 - Para-substituted Mono-alkylpbenol Test Plan for Environmental Fate and Ecotoxicity Endpoints

Phenol	CAS No.	Environmental Fate and Pathway				Ecotoxicology		
		Photo-degradation	Stability in water	Transport/ Distribution - fugacity model	Biodegradation	Acute Fish	Acute Algae	Acute Invertebrate
p-tert-Butylphenol	98-54-4	C	*	C	D	C/D	C/D	C/D
p-sec-Butylphenol	99-71-8	C	*	C		c m	C	C/D
p-tert-Amylphenol	80-46-6	C	*	C	s	C	C	C/D
Heptyl derivs (p-heptylphenol)	72624-02-3	C	*	C	S	C/D	C/D	C R)
p-tert-Octylphenol	140-66-9	D	*	C	D	C/D	C/D	C/D
p-Octylphenol	1806-26-4	C	*	C	S	C	C	C
	599-64-4	C	*	C	S	C	C	C
p-Nonylphenol	84852-15-3	C	*	C	D	C/D	C/D	C/D
p-Dodecylphenol	210555-94-5	D	*	C	D	C/D	C/D	C/D

Key: * = although no studies on abiotic hydrolysis were found, no testing is proposed because the category phenols do not possess any functional groups that are regarded as being susceptible to hydrolysis under environmental conditions.
D = endpoints fulfilled using adequate existing experimental data C = endpoints fulfilled using calculated data S = endpoints fulfilled using category approach (read across)

TEXT = Revision

TABLE 18 - Para-substituted Mono-alkylphenol Test Plan for Mammalian Toxicity Endpoints

Phenol	CAS No.	TOXICOLOGY					
		Acute toxicity	Genetic toxicity - bacterial	Genetic toxicity – non bacterial – *in vivo*	Genetic toxicity – non bacterial – *in vitro*	Repeated toxicity	Repro/ Developmental Toxicity
p-tert-Butylphenol	98-54-4	D	D	S	D	D	D
p-sec-Butylphenol	99-71-8	D	D	S	D	S	S
p-tert-Amylphenol	80-46-6	S	D	S	S	S	S
Heptyl derivs (p-heptylphenol)	72624-02-3	D	D	S	S	S	S
p-tert-Octylphenol	140-66-9	D	D	S	S	D	D
p-Octylphenol	1806-26-4	D	S	S	S	S	S
p-(alpha, alpha-Dimethylbenzyl)phenol	599-64-4	D	D	S	S	S	S
p-Nonylphenol	84852-15-3	D	D	D	D	D	D
p-Dodecylphenol	210555-94-5	D	S	S	S	S	S

Key: S = endpoints fulfilled using category approach (read across)
D = endpoints fulfilled using adequate existing experimental data
T = testing required

TEXT = Revision

TABLE 19 - Di- and Tri-substituted Mixed Alkylphenols Test Plan for Physical Chemistry Endpoints

Phenol	CAS No.	Physical Chemistry Properties				
		Melting Point	Boiling Point	Vapour Pressure	Log Kow	Water Solubility
2,3,6-Trimethylphenol	2416-94-6	D	D	D	D	D
2,4-Di-*tert*-butylphenol	96-76-4	D	D	D	D	D
2,6-Di-*tert*-butylphenol	128-39-2	D	D	D	D	D
2,4-Di-*tert*-pentylphenol	120-95-6	D	D	D	D	D
4-*sec*-Butyl-2,6-di-*tert*-butylphenol	17540-75-9	D	D	D	D	D
2,4,6-Tri-*tert*-butylphenol	732-26-3	D	D	D	D	D
2,4- Bis(alpha, alpha-dimethylbenzyl)phenol	2772-45-4	D	D	D	D	D

Key C = endpoints fulfilled using calculated data D = endpoints fulfilled using adequate existing experimental data T = Testing Proposed

TEXT = Revision

TABLE 20 – Di- and Tri-substituted Mixed Alkylphenols Test Plan for Environmental Fate and Ecotoxicity Endpoints

Phenol	CAS No.	Environmental Fate and Pathway				Ecotoxicology		
		Photo-degradation	Stability in water	Transport/ Distribution – fugacity model	Biodegradation	Acute Fiih	Acute Algae	Acute Invertebrate
2,3,6-Trimethylphenol	24 16-94-6	D	*	C	D	C/D	C/D	C/D
2,4-Di-*tert*-butylphenol	96-76-4	C	*	C	D	C/D	C	C
2,6-Di-*tert*-butylphenol	128-39-2	C/D	*	C	D	C/D	C/D	C1D
2,4-Di-*tert*-pentylphenol	120-95-6	C	*	C	S	C	C	C
4-*sec*-Butyl-2,6-di-*tert*-butylphenol	17540-75-9	C	*	C	S	C	C	C
2,4,6-Tri-*tert*-butylphenol	732-26-3	C	*	C	S	C	C	C
2,4-	2772-45-4	C	*	C	S	C	C	C

Key: * = although no studies on abiotic hydrolysis were found, no testing is proposed because the category phenols do not possess any functional groups that are regarded as being susceptible to hydrolysis under environmental conditions.
D = endpoints fulfilled using adequate existing experimental data
C = endpoints fulfilled using calculated data
S = endpoints fulfilled using category approach (read across)
T = Testing Proposed

TEXT = Revision

TABLE 21 - Di- and Alkylphenols Test Plan for Mammalian Toxicity Endpoints

Phenol	CAS No.	TOXICOLOGY					
		Acute toxicity	Genetic toxicity - bacterial	Genetic toxicity – non bacterial – *in vivo*	Genetic toxicity – non bacterial – *in vitro*	Repeated toxicity	Repro/ Developmental Toxicity
2,3,6-Trimethylphenol	2416-94-6						
2,4-Di-*tert*-butylphenol	96-76-4						
2,6-Di-*tert*-butylphenol	128-39-2						
2,4-Di-*tert*-pentylphenol	120-95-6						
4-*sec*-Butyl-2,6-di-*tert*-butylphenol	17540-75-9						
2,4,6-Tri-*tert*-butylphenol	732-26-3						
2,4-	2772-45-4						

Key: S = category approach (read across)
D = using adequate existing experimental data
T = Testing Proposed

TEXT = Revision

INDUSTRIAL MANUFACTURING AND COMMERCIAL APPLICATIONS OF ALKYLPHENOLS

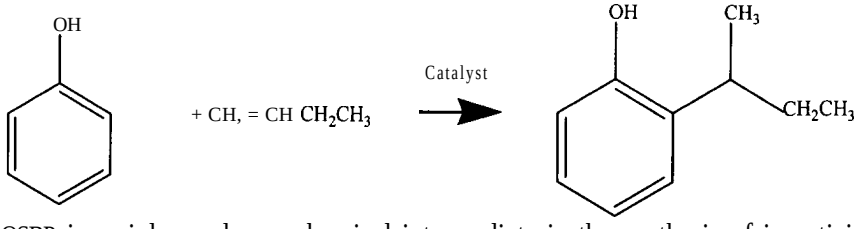
Group I: Ortho-Substituted Mono-Alkylphenols

o-sec-Butylphenol (2-sec-butylphenol)

2-*sec*-Butylphenol (OSBP) CAS RN: 89-72-5, can be produced by two different processes. Both processes have been engineered to comply with applicable environmental regulations using fully automated, closed systems. The choice of process is based on business considerations.

In the first process, a mixture of 1-butene and phenol is passed through a fixed bed of ion exchange resin. The crude alkylphenol, containing phenol, set-butylphenol isomers and other alkylates is rectified by vacuum fractional distillation. In the other process, 1-butene is metered into a solution of a homogeneous catalyst in phenol. Again the crude alkylphenol is rectified by fractional vacuum distillation to achieve the required OSBP purity. Both processes are depicted by the chemical equation in Figure 1.

Figure 1 – Synthesis of OSBP

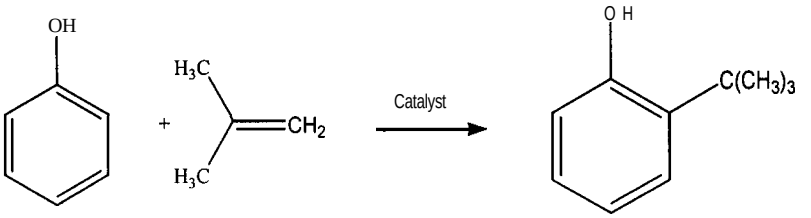


OSBP is mainly used as a chemical intermediate in the synthesis of insecticides, herbicides and as a polymerization inhibitor. It undergoes reactions on the aromatic ring and the phenolic hydroxyl group. It is somewhat less acidic than phenol.

2-tert-Butylphenol

The manufacturing process for 2-*tert*-butylphenol (*ortho-tertiary* butylphenol, OTBP), CAS RN = 88-18-6, has been engineered to comply with applicable environmental regulations using a fully automated, closed system. Phenol and an appropriate *ortho*-alkylating catalyst are charged to a reactor followed by the controlled addition of isobutylene to generate a crude alkylate. See Figure 2. When the reaction is complete, the catalyst is removed from the mixture and the product is recovered at the required quality by fractional vacuum distillation.

Figure 2 – Synthesis of OTBP

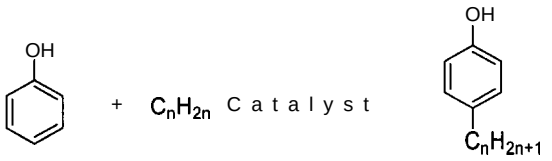


OTBP is used as a starting material for the synthesis of flavor and fragrance chemicals, antioxidants, insecticides, and phenolic resins. Compounds for the fragrance industry can be made from cis-2-*tert*-butylcyclohexanol [72 that is obtained by hydrogenation of OTBP in the presence of Pd/Al_2O_3 or Ru/Al_2O_3 catalysts.

Group II: Para-Substituted Mono-Alkylphenols

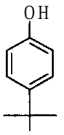
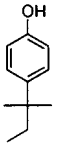
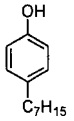
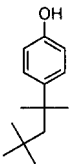
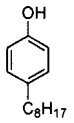
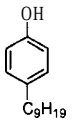
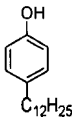
The *para*-substituted alkylphenols are typically made from an olefin and phenol using an acid catalyst (Figure 3). The side chains tend to be highly branched with predominately a tertiary carbon attached to the phenol ring. In some cases, a small amount of ortho isomer is co-produced and must be removed in a purification step. The olefins are either a relatively pure, low molecular weight material with an α-olefin structure such as for PTBP, PTAP, and PTOP or a mixture of isomeric olefins as for PHP, POP, PNP and PDDP. (See Table 22).

Figure 3 - Synthesis of para-substituted alkylphenols



The manufacturing processes for the various *para*-substituted alkylphenols are conducted in fully automated, closed systems that have been engineered to comply with applicable environmental laws and regulations. In the typical reaction, a fixed bed reactor containing a solid acid catalyst is fed with phenol and olefin at the appropriate ratio to produce a mixture of *ortho*- and *para*-alkylphenol and a small amount of by-products. The product is recovered at the required quality by fractional vacuum distillation.

Table 22 – Structure, manufacture and commercial applications of *para*-substituted alkylphenols

Compound	Name	CAS NO.	Starting Olefin	Structure	Applications
PTBP	*p-tert*-Butylphenol	98-54-4	Isobutylene		Phosphate esters, fragrances, oil field chemicals, demulsifiers, polycarbonate chain terminator, glycidyl ethers
PSBP	*p-sec*-Butylphenol	99-71-8	1-Butene		Intermediate in the synthesis of antioxidants and also as a co-solvent
PTAP	*p-tert*-Amylphenol	8046-6	Isoamylene		Demulsifiers, biocides, fragrances
PHP	Heptyl derivs (*p*-Heptylphenol)	72624-02-3	Heptylene		Oil additive intermediate, phenolic resins
PTOP	*p-tert*-Octylphenol	140-66-9	Diisobutylene		Surfactants, tackifier resins, ink resins, polycarbonate chain terminator, ultraviolet stabilizers
POP	p-Octylphenol	1806-26-4	Octene		Surfactants, phenolic resins
PNP	p-Nonylphenol	84852-15-3	Nonene		Demulsifiers, antioxidant intermediate, surfactants, epoxy resin hardener, heat stabilizer for PVC , phenolic resins
PDDP	p-Dodecylphenol	210555-94-2	Dodecene		Surfactants, lube oil additives, intermediate, phenolic resins

In response to EPA's request for further detail on the composition of PHP, POP, PNP, and PDDP below are descriptions of the commercial products.

p-Heptylphenol (PHP)

p-Heptylphenol is manufactured by reacting phenol and "heptene" with an acid catalyst. The heptene used is a mixture of branched C_7H_{14} alkenes that is predominantly alpha olefin. The heptene mixture consists of approximately 12 isomers representing at least 2% each. All of the heptene is branched. The commercial product is a mixture that can be categorized into three major products: ortho-heptylphenol (~2%) 2,4-di-heptylphenol (~7%) and para-heptylphenol (~90%). Each category of alkylated product has numerous isomers. No straight-chained isomers are formed in the process.

p-Octylphenol (POP)

p-Octylphenol is manufactured by reacting phenol and "octene" with an acid catalyst. The octene used is a mixture of branched C_8H_{16} alkenes that is predominantly alpha olefin. The octene mixture consists of approximately 15 isomers representing at least 2% each. The commercial product is a mixture that can be categorized into three major products: ortho-octylphenol (~2%), 2,4-di-octylphenol (~7%) and para-octylphenol (~90%). Each category of alkylated product has numerous isomers. No straight-chained isomers are formed in the process. After 2002, this product will no longer be manufactured due to the fact that this raw material mixture of octene isomers is no longer available.

p-Nonylphenol (PNP)

p-Nonylphenol is manufactured by reacting phenol and "nonene" with an acid catalyst. The nonene used is a mixture of branched C_9H_{18} alkenes that is predominantly alpha olefin. Commercial nonene also contains a small amount of branched decene isomers. The nonene mixture consists of approximately 18 isomers representing at least 2% each. The commercial product is a mixture that can be categorized into four major products: ortho-nonylphenol (~4%), decylphenol (~4%), 2,4-di-nonylphenol (~0.2%) and para-nonylphenol (~90%). Each category of alkylated product has numerous isomers. No straight-chained isomers are formed in the process.

p-Dodecylphenol (PDDP)

p-Dodecylphenol is manufactured by reacting phenol and "dodecene" with an acid catalyst. The dodecene used is a mixture of branched $C_{12}H_{24}$ alkenes that is predominantly alpha olefin. Commercial dodecene also contains a small amount of branched undecene and tridecene isomers. The dodecene mixture consists of approximately 24 isomers representing at least 2% each. The commercial product is a mixture that can be categorized into five major products: ortho-dodecyl phenol (~3%), 2,4-di-dodecylphenol (~1.5%), undecylphenol (~2%), tridecylphenol (~1%) and para-dodecylphenol (~91%). Each category of alkylated product has numerous isomers. No straight-chained isomers are formed in the process.

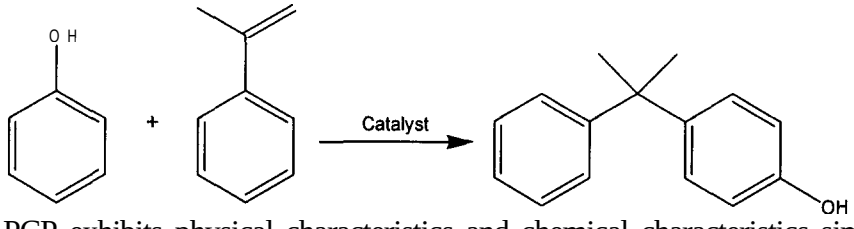
Alkylphenols tend to darken on contact with iron and oxygen. These materials must be stored and shipped in stainless steel vessels under an inert atmosphere. Contact with carbon steel should be avoided.

The commercial uses of the *para*-substituted alkylphenols are numerous and many are listed in Table 22. Typical applications include the use of the alkylphenols as intermediates in the synthesis of primary and secondary antioxidants, demulsifiers, surfactants, lube oil additives, biocides, fragrances, and various types of tackifier, ink and phenolic resins. They also find use as polymerization inhibitors, epoxy resin hardeners, heat stabilizers, and polycarbonate chain terminators.

p-(alpha, alpha-Dimethylbenzyl)phenol (4-cumylphenol)

The manufacturing process for 4-cumylphenol [PCP, *para*-cumylphenol, *p-(alpha, alpha*-dimethylbenzyl)phenol4-(1-methyl-1-phenylethyl)phenol], CAS RN = 599-64-4, is conducted in a fully automated, closed system that has been engineered to comply with applicable environmental regulations. An appropriate blend of phenol and 2-methylstyrene [a-methylstyrene, AMS] is passed through a fixed-bed of a solid acid catalyst. The crude alkylphenol stream containing phenol, cumylphenol isomers and reaction byproducts is rectified by vacuum fractional distillation to achieve the required purity for PCP. The process is depicted by the chemical equation in Figure 4.

Figure 4 – Synthesis of PCP



PCP exhibits physical characteristics and chemical characteristics similar to those of other para-alkylated phenols. PCP is used as a chemical intermediate in the synthesis of specialty surfactants and phenolic resins. Its primary use is as a chain-stopper in polycarbonate resins to control molecular weight and physical properties.

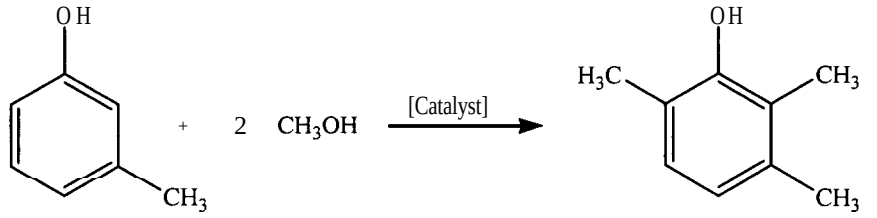
Group III Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol

The manufacturing process for 2,3,6-trimethylphenol (TMP), CAS RN = 2416-94-6, is conducted in an automated, closed system that has been engineered to comply with applicable environmental regulations. A fixed bed reactor containing a mixed metal oxide catalyst is fed with a mixture of methanol and 3-methylphenol. The product is separated

from the byproduct, water, then distilled under fractional vacuum distillation to achieve the quality required. See Figure 5.

Figure 5 – Synthesis of 2,3,6-TMP



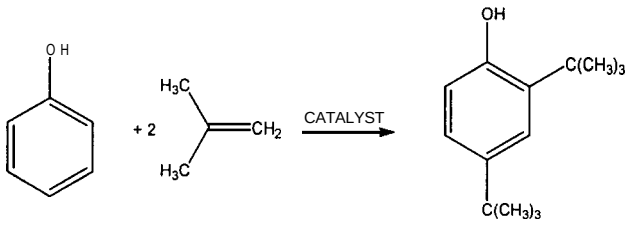
2,3,6-TMP is an intermediate in synthetic Vitamin E, in antioxidants and in polymer applications. Each application involves the susceptibility of the phenolic ring to oxidation. Under normal storage conditions, 2,3,6-TMP is blanketed with an inert gas to mitigate the reaction between atmospheric 0_2 and 2,3,6-TMP.

2,3,6-TMP also displays another characteristic of phenols. It has a weakly acidic proton which can react with bases.

2,4-Di-tert-butylphenol

The manufacturing process for 2,4-di-*tertiary*-butylphenol (2,4-DTBP), CAS RN = 96-76-4, is conducted in a fully automated, closed system that has been engineered to comply with applicable environmental regulations. A reactor is first charged with phenol and an acid catalyst. Then isobutylene is added into the reaction under controlled conditions to generate a crude alkylate. The crude alkylate contains 2,4-DTBP, mono- and tri-butylphenol, some isomers and by-products. The catalyst is separated from this alkylate. The product is recovered at the required quality by fractional vacuum distillation. The chemical equation for the process is shown in Figure 6.

Figure 6 – Synthesis of 2,4-DTBP



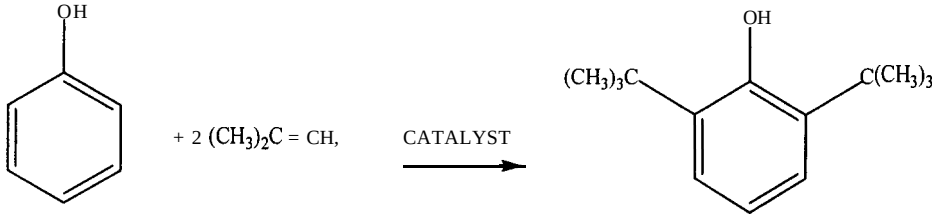
The primary use of 2,4-DTBP is in the synthesis of triaryl phosphites. These are used as secondary antioxidants, primarily in plastics. 2,4-DTBP also can be used to produce primary phenolic antioxidants by condensing it with an aldehyde at the ortho position to produce a high molecular weight bisphenolic, which stabilizes polyolefins, styrenics and natural or

synthetic rubber. 2,4-DTPB can also be converted benzotriazole derivatives or an ester of 3,5-di-tert-butyl-4-hydroxybenzoic acid, both of which are used as UV stabilizers.

2,6-Di-tert-butylphenol

The manufacturing process for 2,6-di-*tert*-butylphenol (2,6-DTBP), CAS RN = 128-39-2, is conducted in a fully automated, closed system that has been engineered to comply with applicable environmental regulations. An autoclave reactor is first charged with phenol and catalyst. Then isobutylene is added into the reaction under controlled conditions to generate a crude alkylate. The catalyst is separated from this alkylate. The product is recovered at the quality required by fractional vacuum distillation. See Figure 7.

Figure 7 – Synthesis of 2,6-DTBP



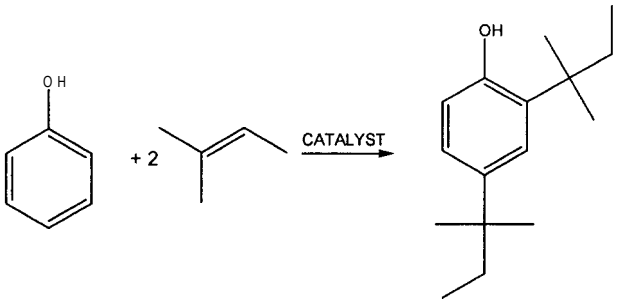
Like other alkylphenols, 2,6-DTBP is susceptible to discoloration in air. This is the result of an oxidation reaction with oxygen. The presence of two ortho-tert-butyl groups stabilizes the phenoxy radical generated by oxidation. This stabilizing influence also explains the good antioxidant property of 2,6-DTBP.

2,6-DTBP can be used as an antioxidant, and it is an important commercial building block for hindered phenolic antioxidants. In these applications, reactions are carried out at the 4-position of 2,6-DTBP to impart a desirable characteristic, such as solubility or reduced volatility, to the antioxidant. 2,6-DTBP can be utilized as a starting material in the synthesis of 4,4'-biphenol. Two molecules of 2,6-DTBP are oxidatively coupled under appropriate conditions to the tetra-substituted biphenol. The butyl groups are subsequently cleaved from the ring to generate the biphenol.

2,4-Di-tert-pentylphenol (2,4-Di-tert-amylphenol)

The process for manufacturing 2,4-di-*tertiary*-amylphenol [2,4-DTAP; 2,4-bis(1,1-dimethylpropyl)phenol], CAS RN = 120-95-6, is conducted in a fully automated, closed system that has been engineered to comply with applicable environmental regulations. First, a reactor is charged with phenol and an acidic catalyst. Then isoamylene (a 90/10 mixture of 2-methyl-2-butene and 2-methyl-1-butene) is added into the reaction under controlled conditions to generate a crude alkylate. The crude alkylate contains 2,4-DTAP, mono- and tri-amylphenol, some isomers and by-products. The catalyst is separated from this alkylate. The product is recovered at the required quality by fractional vacuum distillation. The chemical equation for the process is shown in Figure 8.

Figure 8 – Synthesis of 2,4-DTAP

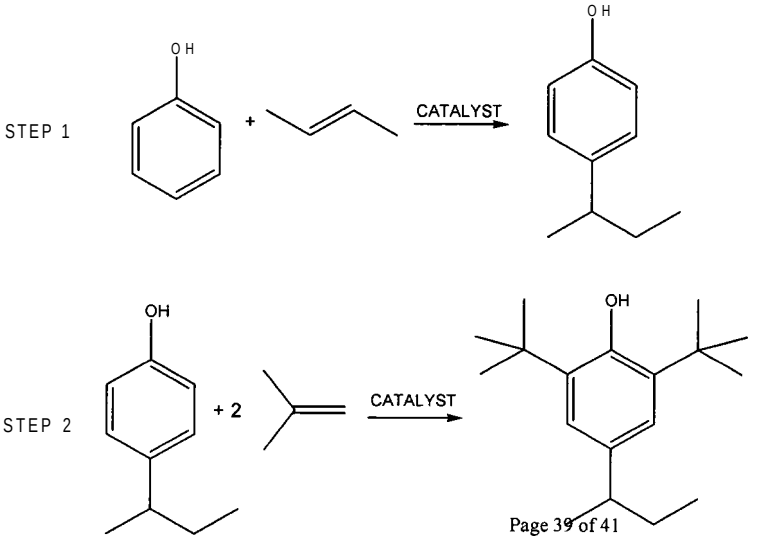


The major use of 2,4-DTBP is in the production of UV stabilizers. The major one is a benzotriazole-based UV absorber used in polyolefin films, outdoor furniture and automotive clear coat finishes. A number of phenoxyacetic acid derivatives are used in the photographic industry. Reaction with ethylene oxide produces a speciality surfactant that can be used to treat cotton fibres. A similar product can be used as a fuel additive acting as a corrosion inhibitor.

4-sec-Butyl-2,6-di-tert-butylphenol (ISONOX® 132)

The process for manufacturing ISONOX® 132 [2,6-di-*tert*-4-*sec*-butylphenol], CAS RN = 17540-75-9, is a two-step process that is conducted in fully automated, closed systems that have been engineered to comply with applicable environmental regulations. In the first step, a fixed bed reactor containing a solid acid catalyst is charged with phenol and 2-butene to produce a mixture of ortho- and *para-sec*-butylphenol (OSBP & PSBP). This mixture is rectified by distillation. In the second step, the purified PSBP, isobutylene, and an appropriate catalyst are added in a reactor under controlled conditions to generate a crude alkylate. The crude alkylate is separated from the catalyst. The product is recovered at the required quality by fractional vacuum distillation. The chemical equation for the process is shown in Figure 9.

Figure 9 – Synthesis of ISONOX® 132

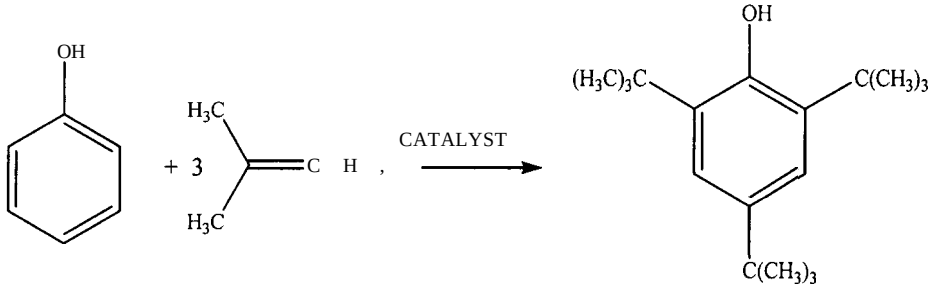


The primary use of ISONOX® 132 is as an antioxidant. It is a low cost, highly active liquid stabilizer for polyols, PVC, polyurethane, adhesives and functional fluids. ISONOX® 132 has received FDA approval for use as an antioxidant in indirect food contact applications in plasticized vinyl chloride homo- and copolymers (PVC).

2,4,6-Tri-*tert*-butylphenol

The manufacturing process for 2,4,6-tri-*tert*-butylphenol (2,4,6-TTBP), CAS RN = 732-26-3, is conducted in a fully automated, closed system that has been engineered to comply with applicable environmental regulations. An autoclave reactor is first charged with phenol and catalyst. Then isobutylene is added into the reaction under controlled conditions to generate a crude alkylate. See Figure 10. The catalyst is separated from this alkylate. The product is recovered at the quality required by either fractional vacuum distillation or recrystallization in an appropriate solvent.

Figure 10 – Synthesis of 2,4,6-TTBP

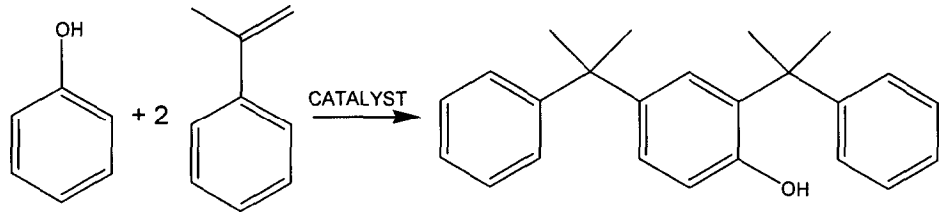


Like most alkylphenols with bulky substituents, 2,4,6-DTBP can be used as a primary antioxidant or as an intermediate in the synthesis of primary antioxidants. Its primary commercial use, however, is an intermediate in the synthesis of polymer stabilizers that provide enhanced hydrolytic, thermal oxidative, and UV stability to thermoplastic resins.

2,4- Bis(alpha, alpha- dimethylbenzyl)phenol (2,4-dicumylphenol)

The manufacturing process for 2,4-dicumylphenol [2,4-DCP; 2,4-*bis*(1 -methyl-l - phenethyl)phenol], CAS RN = 2772-45-4, is conducted in a processing unit that has been engineered to comply with applicable environmental regulations. a-Methylstyrene (AMS) is added into a reactor containing phenol and an acidic catalyst at a controlled rate. Once the reactor contents have reached the desired composition, the catalyst is separated from the crude alkylate. This material, containing mono-cumylphenol isomers, DCP and byproducts is rectified by fractional vacuum distillation to achieve the desired purity. The process is shown in Figure 11.

Figure 11 – Synthesis of 2,4-DCP



The predominant use 2,4-DCP is as a chemical intermediate. In its primary use, 2,4-DCP is converted to a benzotriazole to produce a UV stabilizer. It can also be used as a primary antioxidant or can be converted to a secondary antioxidant as a phosphite. In each case, the material is used in high temperature polymers where higher thermal stability is needed during high temperature molding processes.